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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,063	08/27/2001	Michael J. Briskin	1855.1070-004	3846

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,063	BRISKIN ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,21-47,53,60,84,88,97-109 and 111-115* is/are pending in the application.

4a) Of the above claim(s) *16,47,53,60 and 115* is/are withdrawn from consideration.

5)☒ Claim(s) *28-33* is/are allowed.

6)☒ Claim(s) *21-26, 34-46, 84, 97-102, 109, and 113-114* is/are rejected.

7)☒ Claim(s) *27,88,103-108,111 and 112* is/are objected to.

8)☒ Claim(s) *16,21-47,53,60,84,88,97-109 and 111-115* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

JL

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

1. The amendment and response filed 30 December 2004 has been received and entered in full. Claims 116-121 have been cancelled, and claims 16, 21, 23-26, 34-37, 39, 41, 43, 46-47, 53, 60, 84, 97-102, 109, and 113-115 have been amended.

2. Applicant's request for rejoinder of claims 16, 47, 53, 60, and 115 in accordance with MPEP §821.04 is acknowledged. However, rejoinder of the process claims will be deferred until all of the pending product claims are found allowable. Therefore, claims 16, 21-47, 53, 60, 84, 88, 97-109, and 111-115 are pending and claims 21-46, 84, 88, 97-109, and 111-114 are the subject of this Office Action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the previous Office Action mailed 28 July 2004.

Information Disclosure Statement

4. Applicant's Supplemental IDS, filed 30 December 2004, is acknowledged.

Withdrawn Objections And/Or Rejections

Claim Rejections - 35 USC § 112, 2nd Paragraph

5. The rejection of claims 116-121 under 35 U.S.C. §112¶2 as set forth at pages 4-5 of the previous Office Action (mailed 28 July 2004) is moot in view of Applicant's cancellation of said claims (filed 30 December 2004).

Claim Rejections - 35 USC § 112, 1st Paragraph (Written Description)

6. The rejection of claims 21-27, 34-46, 84, 88, 97-109, and 111-114 under 35 U.S.C. § 112, First Paragraph as set forth at pages 4-5 regarding the genus SExCKine and pages 5-6 regarding mammalian ligands and chemokine ligands of the previous Office Action (mailed 28 July 2004) is withdrawn in view of Applicant's amendment of said claims that now recite specific ligands (filed 30 December 2004).

Double Patenting

9. The rejection of claims 21-46, 84, 88, and 97-114 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21, 28, 31, 34, 197-201, 203, 205, and 206 of copending U.S. Application No. 10/174,293 is withdrawn in view of Applicant's cancellation of claims 21, 28, 31, 34, 197-201, 203, 205, and 206 in copending U.S. Application No. 10/174,293.

Maintained and New Objections/Rejections

Claim Objections

10. Claim 109 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 44. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112, 1st paragraph (Enablement)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 24-26, 35-37, 41-43, 45-46, 97-102, and 113-114 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an antibody or antigen-binding fragment thereof which binds mammalian BONZO and inhibits the binding of a ligand to said BONZO, wherein said ligand is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8 (and recited fragments thereof), wherein said antibody or antigen-binding fragment inhibits chemotaxis in response to binding of said ligand to said BONZO, does not reasonably provide enablement for an antibody or antigen-binding fragment thereof which binds mammalian BONZO and inhibits the binding of a ligand to said BONZO, wherein said

ligand is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8 (and recited fragments thereof), wherein said antibody or antigen-binding fragment inhibits a cellular response selected from the group consisting of proliferation, migration, chemotaxis, secretion, exocytosis, degranulation, inflammatory mediator release, respiratory burst, and Ca^{2+} flux, or an antibody or antigen-binding fragment thereof which binds mammalian BONZO and inhibits the binding of a ligand to said BONZO, wherein said ligand is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8 (and recited fragments thereof), wherein said antibody or antigen-binding fragment inhibits chemotaxis that *is not* in response to binding of said ligand to said BONZO. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

12. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

13. Claims 24, 35, 43, 97-102 recite "wherein said antibody or antigen-binding fragments inhibits signal transduction and/or a cellular response". Although the claims set forth that the signal transduction and/or cellular response is the result of the binding of the specific ligands recited in claim 21, the claims are drawn very broadly to inhibiting any signal transduction

mechanism or cellular response (See 112(2) rejection below). Claims 25 and 36 recite "wherein said antibody or antigen-binding fragment inhibits a cellular response selected from the group consisting of proliferation, migration, chemotaxis, secretion, exocytosis, degranulation, inflammatory mediator release, and respiratory burst", claims 26 and 37 recite "wherein said antibody or antigen-binding fragment inhibits a cellular response, and said cellular response is chemotaxis". The claims do not require that the cellular response is the result of the binding of the specific ligands recited in claim 21, for example. Claim 41 recites an antibody or antigen-binding fragment thereof which binds mammalian BONZO expressed on the membrane of a cell and inhibits a cellular response to binding of a ligand to said BONZO. Although the claim sets forth that the cellular response is the result of the binding of the specific ligands recited in claim 21, for example, the claim is drawn very broadly to inhibiting any cellular response. Claim 42 recites an antibody or antigen-binding fragment thereof which binds mammalian BONZO expressed on the membrane of a cell and inhibits a cellular response to binding of a ligand to said BONZO, wherein said cellular response is selected from the group consisting of Ca2+ flux, chemotaxis, exocytosis, and respiratory burst. Lastly, claims 113 and 114 recite "wherein said antibody or antigen-binding fragment inhibits transient increase in the concentration of cytosolic free calcium induced upon binding of ligand to said BONZO". Although the claims set forth that the cellular response of an increase in the concentration of cytosolic free calcium is the result of the binding of the specific ligands recited in claims 21 and 34, respectively, the specification has not taught that binding of said ligands results in an increase in the concentration of cytosolic free calcium. While the Specification discloses antibodies that bind mammalian BONZO and inhibit SExCkine induced chemotaxis, it does not teach a commensurate number of the claimed cellular

responses that are inhibited by said antibodies. Based upon the limited cellular responses that are inhibited by said antibody, it is not at all predictable that the disclosed antibody would inhibit all of the cellular responses recited in the claims, and undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 2nd paragraph

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 24, 35, 43, and 97-102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. Claims 24, 35, 43, and 97-102 are indefinite for reciting the phrase "signal transduction and/or a cellular response" as recited in each of the claims. Since the last part of each claim recites "in an *in vitro* chemotaxis assay", it is unclear what is encompassed by the phrase "signal transduction and/or a cellular response.

Claim Rejections - 35 USC § 102

17. Claims 21-26, 34-46, 97-102, 109, and 113-114 remain rejected under 35 U.S.C. 102(b) as being anticipated by Farber et al. (WO 98/44098, IDS #AP, see entire document) for reasons set forth in the previous Office Action (mailed 28 July 2004).

18. Applicant's arguments filed filed 30 December 2004 have been fully considered but they are not persuasive. Applicants argue at page 22 of the response that Farber et al. do not actually

teach or exemplify an particular anti-STRL33 antibodies that are capable of blocking membrane fusion between HIV and target cells, they only suggest that such an antibody might be produced. This argument has been fully considered but is not deemed persuasive because although Farber et al. fully disclose the antibodies of their invention (See pages 26, line 10 through page 33, line 5). It is not necessary that Farber et al. provide working examples. Applicants argue at pages 22-24 that Farber et al. do not expressly teach an antibody or antigen-binding fragment which binds mammalian Bonzo and inhibits the binding of the specific recited ligands (SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8). Applicants also cite a number of references (Lee et al., Wu#1, Wu#2) which report that various monoclonal antibodies that bind CCR5, another chemokine receptor which, like Bonzo, is a coreceptor for HIV-1 cellular entry, show differential effects on the binding of HIV-1 envelope binding and chemokine binding. This argument has been fully considered but is not deemed persuasive for reasons set forth at pages 8-9 (¶ 33-34) of the previous Office Action (mailed 28 July 2004). Furthermore, the references cited by Applicants demonstrate that CCR5 has several immunodominant epitopes, and that monoclonal antibodies to the second extracellular loop or CCR5 were more effective at blocking chemokine binding than HIV-1 envelope binding, while other monoclonal antibodies to the amino terminal domain of CCR5 blocked gp120 binding but had little or no effect on chemokine binding. Therefore, while the art teaches that certain monoclonal antibodies demonstrate differences in their abilities to inhibit chemokine/HIV-1 binding to CCR5, it does not show that antibodies that block HIV-1 binding would necessarily have no effect on chemokine binding. In fact, the Lee et al. reference teaches that antibody 2D7 blocked both chemokine binding and HIV-1 envelope binding (See Lee et al., Abstract, for example). More importantly, it is noted that the antibodies

taught by Farber et al. are not limited to antibodies that bind STRL33 and inhibit binding of HIV-1, but include antibodies of different epitopic specificities (See page 26, lines 22-25). Therefore, the antibodies taught by Farber et al., which includes antibodies that bind STRL33 and inhibit binding of HIV-1 to Bonzo, would, in the absence of evidence to the contrary, inhibit binding of any other ligand to Bonzo. Since the Office does not have the facilities for examining and comparing Applicants' antibody with the antibodies of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the antibody of the prior art does not possess the same material structural and functional characteristics of the claimed antibody). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

19. Claim 84 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Farber et al. in view of Jardieu et al. (U.S. Pat. No. 6,037,454).

20. Applicant's arguments filed 30 December 2004 have been fully considered but they are not persuasive. Applicants argue at 25 that Farber et al. do not expressly or inherently teach or suggest the claimed antibodies and antigen binding fragments and the teachings of Jardieu et al. do not teach or suggest the claimed antibodies of antigen-binding fragments. This arguments has been fully considered but is not deemed persuasive for the reasons stated in the 102(b) rejection *supra.* Therefore, the rejection of claim 84 under 35 U.S.C. 103(a) as being unpatentable over

Farber et al. in view of Jardieu et al. (U.S. Pat. No. 6,037,454) is maintained for reasons stated at pages 9-10 (¶ 35-43) of the previous Office Action (mailed 28 July 2004).

Allowable Subject Matter

21. Claims 27, 88, 103-108, 111-112 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

22. Claims 28-33 remain allowable as the prior art does not teach or suggest the particular species of antibodies and cell lines producing said antibodies.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
April 15, 2005

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER